

REMARKS

With entry of the amendment, claims 1-21 are pending. Claims 1-11 are under consideration, and claims 12-21 are withdrawn as being drawn to a non-elected invention. Claims 1-3 and 5-11 are rejected, and claim 4 is objected to as depending from a rejected base claim.

Applicants have amended claim 5 to recite a polypeptide having at least 95% amino acid identity. The amendment is fully supported by the specification as filed, introduces no new matter, and does not necessitate a new search.

In view of the amendments above and arguments below, Applicants respectfully request allowance of claims 1-11.

Rejection under 35 U.S.C. 112, first paragraph

Claim 5 is rejected under 35 U.S.C. 112, first paragraph as not being enabled for the scope of the claim. Claim 5 is drawn to an isolated polypeptide having at least 70% amino acid identity and having the ability to bind to and cleave C1-esterase inhibitor.

Applicants have amended claim 5 to recite a polypeptide comprising at least about 95% amino acid identity to SEQ ID NO:2. Support for the amendment is found, for example, at page 7, line 5. Applicants respectfully submit that claim 5, as currently amended, is fully enabled by Applicants' disclosure.

Applicants' invention is a pioneering discovery. Applicants were the first to isolate and characterize StcE, a protein expressed by most enterohemorrhagic *Eschericia coli* isolates, including the potentially deadly *E. coli* O157:H7 strain. Applicants were the first to discover that the protein is, in fact, expressed *in vivo* and that it may be involved in infectivity or pathogenesis of pO157-positive strains of *Eschericia coli*. Using the teachings of the specification, one of ordinary skill in the art could design and produce sequences having at least about 95% identity to SEQ ID NO:2 and screen for binding to and cleavage of C-1 esterase inhibitor without undue experimentation, particularly in light of Applicants' having disclosed a region required for cleaving C-1 esterase inhibitor (amino acids 434-444 of SEQ ID NO:2) and screening tests to permit one of ordinary skill in the art to determine whether a particular sequence falls within the scope of the claims.

Applicants respectfully submit that their discovery represents a significant advance over the prior art in this area of endeavor. Applicants are entitled to claims of a slightly broader scope, which are necessary to afford meaningful protection of this pioneering invention.

Applicants respectfully request that the rejection under 35 U.S.C. 112, first paragraph be withdrawn.

Rejections under 35 U.S.C. 112, second paragraph

Claims 1-3 and 6-11 are rejected under 35 U.S.C. 112, second paragraph as containing subject matter not described in the specification in such a way as to convey possession of the claimed invention. The Examiner asserts that the claims encompass specific fragments of SEQ ID NO:2 with no associated function.

With all due respect, Applicants disclosed (e.g., at page 6, paragraph 29 of the specification) that polypeptide fragments of SEQ ID NO:2 could function as antigens in developing antibodies. As one of ordinary skill in the art would appreciate, a polypeptide fragment of a larger polypeptide need not retain the function of the larger polypeptide in order to be useful as an antigen. Larger fragments as claimed in claims 1-3 could reasonably be expected to retain activity, and both the larger fragments of claims 1-3 and the smaller fragments of claims 6-11 would be useful for raising StcE-specific antibodies.

Accordingly, Applicants request that the rejection under 35 U.S.C. 112, second paragraph be withdrawn.

Rejections under 35 U.S.C. 102(b)

Claims 1-3 and 6-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Makino *et al.* (DNA Research 5:1-9, 1998) or Burland (Nuc. Acid Res. 26:4196-4204, 1998), and claims 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Brunder (Accession No. Q9ZAL1, May 1, 1999). The Examiner characterized Makino and Burland as disclosing a polypeptide sequence that is 100% identical to SEQ ID NO:2, or comprises the polypeptide or fragments of claims 1-3 and 6-11, and that Brunder teaches a polypeptide sequence having 275 amino acid residues that match SEQ ID NO:2.

Applicants contend that the entire nucleotide sequence of the 92-kb plasmid pO157 has been sequenced. With all due respect, the sequence shown in Makino *et al.* or Burland is merely one of hundreds of hypothetical protein sequences based on deduced amino acid sequences of putative translation products of potential open reading frames found on pO157. Applicants

acknowledge that the sequence of the hypothetical proteins of Makino *et al.* and Burland are the same as SEQ ID NO:2. However, Applicants do not claim SEQ ID NO:2, which is admittedly identical to the deduced amino acid sequences of the putative coding sequences of Burland or Makino *et al.* Rather, Applicants claim an isolated polypeptide comprising SEQ ID NO:2. The art does not teach an isolated polypeptide comprising SEQ ID NO:2.

Claims 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Brunder *et al.* (Accession No. Q9ZAL1, May 1, 1999, IDS reference AS). Brunder is characterized as disclosing a polypeptide sequence having 275 amino acid residues that match SEQ ID NO:2. The polypeptide is said to comprise fragments that have 17, 25, or 40 consecutive amino acids identical to those of SEQ ID NO:2, as required by claims 6-8. In fact, the alignment shows that the sequence disclosed in Brunder is identical to amino acid residues 24-299 of SEQ ID NO:2. Again, Brunder *et al.* discloses the sequence of a hypothetical protein, rather than isolated polypeptides.

In view of the forgoing, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. 102(b).

Although the Examiner has not rejected the claims under 35 U.S.C. 103(a), Applicants wish to emphasize that the cited art provides no teaching or suggestion that would cause one skilled in the art to select for synthesis and isolation the particular *hypothetical* protein sequence from among all the other *hypothetical* protein sequences that may or may not be produced *in vivo*. Applicants discovered a protein (StcE), previously merely one of many hypothetical proteins, which is, in fact, potentially clinically relevant. This discovery was not reached by resort to the burgeoning databanks. Rather, Applicants made this discovery by correlating the loss of an observed phenotype, which Applicants also discovered (i.e., the ability to cause certain types of cells to aggregate), with the disruption of a particular sequence in a transposon mutant. The cited art provides no motivation to one of ordinary skill in the art to make the polypeptides of claims 1-3 or 6-11, because the cited art does not disclose that StcE is, in fact, expressed *in vivo*.

Objection to claim 4

The Examiner has indicated that claim 4 is allowable, but has objected to claim 4 as depending from a rejected base claim. Applicants agree that claim 4 is allowable over the prior art. However, Applicants respectfully submit that it is not necessary to rewrite claim 4 as an independent claim because claim 1, from which claim 4 depends, is also patentable. Accordingly, Applicants request withdrawal of the rejection and allowance of the claims.



As the application is now in condition for allowance, Applicants respectfully request withdrawal of all rejections and allowance of the claims.

This submission is accompanied by check number 50045 in the amount of \$205.00 for the fee required under 37 C.F.R. 1.17a(2). No other fee is believed due in connection with this submission. However, if a fee is owing, please charge such fee to Deposit Account No. 50-0842.

Respectfully submitted,



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